Name: Ella Edginton
Job title: Policy adviser
Organisation / Institution: Royal College of Physicians of London
Is this input submitted as an organisational or individual response? Organisational
Are you happy for your response to be published by the Academy? Yes

Submitted using the online form, now formatted into a PDF.

---

2. When evaluating the risks and benefits of medicinal products, what are the strengths of evidence that originates from different sources?

It is important to emphasise the strength of properly conducted, randomised controlled trials as well as the value of large observational studies especially where there is a weight of evidence to support them. This is an area where guidelines have a good process and maybe one which should be used to explain to the public the strength of evidence which underpins recommendations. However, both RCTs and meta-analyses have weaknesses which need to be accounted for (outlined below).

3. When evaluating the risks and benefits of medicinal products, what are the limitations of evidence that originates from different sources?

In respect of RCTs, there is a risk that because they are seen as the “gold standard” of research, the weaknesses of the specificity of the population involved are often overlooked. It is essential to ask in what context the medicine is to be used, whether the testing was sufficiently robust to provide evidence for that setting and those people, and how confidently one can say from the evidence what potential adverse events might be, since adverse events tend to occur when a medicine is used in a context different from that in which it was trialled. For example, it seems necessary to be more explicit about a study’s ability to detect risk which would be judged differently according to whether there is a preventive treatment to be taken for very prolonged periods or a shorter period with a specific condition already manifest,

In respect of meta-analyses, there is areal danger of believing that such studies can somehow overcome the limitation of the original RCTs, although this is not the case.

Both of these weaknesses serve to underscore the strong need for robust post-marketing surveillance, as it is often at the post market phase, when drugs are used with wider groups of patients than are eligible for any given trial, that adverse events often manifest.

4. Please provide details of any further examples or case studies that it would be useful for the project to consider.

www.jbs3risk.com) be used as a good example. It relates to the use of statins but, more broadly, is an excellent example of how to use new ways of communicating these risks/benefits to patients and the public at an individual level to inform patient choice.

Finally, the review might wish to consider engaging with Professor Sir David Speigelhalter at the University of Cambridge to advise how risks/benefits are best communicated to patients and the public.

5. Please highlight any broadly applicable principles that should govern the presentation, interpretation and weighting of evidence about medicinal products.

This is a difficult area but one where there are good, established ways to evaluate and weight evidence. The manner in which clinical guidelines use a scoring system on the weight of evidence and the strength of the recommendation is a good way to underpin the views of healthcare professionals and could be utilised as a way of demonstrating to the public the strength of evidence and how it should be best interpreted. However, while such standardised approaches are useful, particularly for communicating with the profession, it is important for doctors to be mindful that different language will be necessary for communicating with different people.

It is also important for the Academy to consider the impact of potentially biased, selective or misinformed communication by media and medical journals, which can result in harm to patients. For example, in a survey by the British Cardiovascular Society in September 2014, 59% of 192 respondents said media reports had led patients to discontinue statins where they believed they were indicated.

6. Concerns have been raised about how industry funding impacts on the validity, or the perception of validity, of evidence. For example, the ability of academic researchers funded by industry to remain impartial when evaluating evidence has come into question. How should conflicts of interest be addressed? How important is industry funding in generating and analysing evidence? Other than industry sponsorship, what are other potential sources of conflicts of interest?

The issue of Conflicts of Interest is challenging as many key opinion leaders who are involved in research or the development of recommendations and guidelines have potential conflicts with pharma and other industry partners. It is essential that any COI are transparent, however this may be insufficient to restore and grow public confidence. One of the most important additional measures is that all trial data should be made available, ensuring both that it can be used and built on by other researchers, and also that professionals and the public can be assured that there is no data being hidden or obscured because it may have been contrary to the desired outcome of the original project.

If formal guidelines are to be used as a key vehicle for informing the profession, patients and the public, it may be necessary for evaluation of the evidence in guideline development to be undertaken independently of any pharmaceutical industry conflicts of interest.

It is also important to be mindful that there are many other potential conflicts of interest. For example, a specialty may have a vested interest in Seeing guidelines include test and surveillance measures which promote the need for professionals in their specialty, even where the wider profession may regard this as unnecessary. Consequently there needs to be some mechanism for key professional bodies such as the Royal Colleges and their specialty societies to have input on the content and strength of the recommendations contained within guidelines.

8. What are the most effective ways of communicating evidence to various stakeholders and engaging with them about such evidence?

Here it is important that there is some understanding of who patients and the public trust to advise on recommendations for medical treatment - that is, the relative credibility with which they see the media, the government, healthcare bodies such as NICE, medical journals or professional societies such as Colleges and specialist professional societies. Understanding this might help inform who is best placed to provide advice and recommendations to patients and the public at a national level and how this might best be achieved.